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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/587,052

04/09/2007

Paul A. Bunn Jr.

5941-65-PUS

7009

22442

7590

06/30/2009

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EXAMINER

AEDER, SEAN E

ART UNIT

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DELIVERY MODE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/587,052	Applicant(s) BUNN JR. ET AL.	
	Examiner SEAN E. AEDER	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 June 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 48,49,51-53,55-59 and 66-81 is/are pending in the application.
- 4a) Of the above claim(s) 51,52,59,68-72 and 75 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 48,49,53,55-58,66,67,73,74 and 76-81 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>6/9/09</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/9/09 has been entered.

Claims 48, 49, 51-53, 55-59, and 66-81 are pending.

Claims 51, 52, 59, 68-72, and 75 are withdrawn.

Claims 57, 66, and 76-81 have been amended by Applicant.

Claims 48, 49, 53, 55-58, 66, 67, 73, 74, and 76-81, as drawn to the species "E-Cadherin", are currently under consideration.

Objections Withdrawn

All previous objections are withdrawn.

Rejections Withdrawn

All previous rejections are withdrawn.

New Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 48, 49, 53, 55-58, 66, 67, 73, 74, and 76-81 are rejected under 35 U.S.C.

112, first paragraph, because the specification, while being enabling for a method to select a lung cancer patient who is predicted to benefit from therapeutic administration of gefitinib comprising detecting the level of E-cadherin polynucleotides in a sample of tumor cells from said patient, comparing said level to a level of E-cadherin polynucleotides in a sample of tumor cells from a subject having lung cancer that is resistant to gefitinib, and selecting the patient as being predicted to benefit from therapeutic administration of gefitinib if the level of E-cadherin polynucleotides in the sample of tumor cells from said patient is higher than the level of E-cadherin polynucleotides in the sample of tumor cells from the subject that is resistant to gefitinib, **the specification does not reasonably provide enablement for (1) methods to select a lung cancer patient who is predicted to benefit from therapeutic administration of an EGFR inhibitor selected from the group consisting of gefitinib and erlotinib comprising (a) detecting in a sample of tumor cells from just any patient to be tested (including those without lung cancer), the expression of E-cadherin polynucleotides, (b) comparing the level of expression of E-cadherin polynucleotides detected in the patient sample to a level of expression of E-cadherin polynucleotides that has been correlated with just any type of disorder or condition that has been correlated with sensitivity or resistance to the**

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EGFR inhibitor, and (c) selecting the patient as being predicted to benefit from therapeutic administration of the EGFR inhibitor selected from the group consisting of gefitinib and erlotinib if the expression level of the E-cadherin polynucleotides in the patient's tumor cells is statistically more similar to the expression level of the E-cadherin polynucleotides that has been correlated with sensitivity to the EGFR inhibitor than to resistance to the EGFR inhibitor (see claim 66) or (2) methods of selecting a lung cancer patient who is predicted to benefit from therapeutic administration of an EGFR inhibitor selected from the group consisting of gefitinib and erlotinib comprising selecting just any type of patient with tumor cells expressing any amount of E-cadherin polynucleotide as predicted to benefit from therapeutic administration of the EGFR inhibitor (see claim 57). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *Ex parte* Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The instant claims are broadly drawn to (1) methods to select a lung cancer patient who is predicted to benefit from therapeutic administration of an EGFR inhibitor

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selected from the group consisting of gefitinib and erlotinib comprising (a) detecting in a sample of tumor cells from just any patient to be tested (including those without lung cancer), the expression of E-cadherin polynucleotides, (b) comparing the level of expression of E-cadherin polynucleotides detected in the patient sample to a level of expression of E-cadherin polynucleotides that has been correlated with just any type of disorder or condition that has been correlated with sensitivity or resistance to the EGFR inhibitor, and (c) selecting the patient as being predicted to benefit from therapeutic administration of the EGFR inhibitor selected from the group consisting of gefitinib and erlotinib if the expression level of the E-cadherin polynucleotides in the patient's tumor cells is statistically more similar to the expression level of the E-cadherin polynucleotides that has been correlated with sensitivity to the EGFR inhibitor than to resistance to the EGFR inhibitor and (2) methods of selecting a lung cancer patient who is predicted to benefit from therapeutic administration of an EGFR inhibitor selected from the group consisting of gefitinib and erlotinib comprising selecting just any type of patient with tumor cells expressing any amount of E-cadherin polynucleotide as predicted to benefit from therapeutic administration of the EGFR inhibitor. This includes methods wherein patient samples are from patients without lung cancer. This includes methods wherein levels in patient samples are compared to levels in any type of samples from any type of patient with just any type of disorder or condition that is sensitive to gefitinib or erlotinib. This includes methods wherein any amount of E-cadherin expression in tumor cells of a patient indicates said patient is sensitive to gefitinib or erlotinib.

This invention is in a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology". *Mycogen Plant Sci., Inc. v. Monsanto Co.*, 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The specification teaches a method to select a lung cancer patient who is predicted to benefit from therapeutic administration of gefitinib comprising detecting the level of E-cadherin polynucleotides in a sample of tumor cells from said patient, comparing said level to a level of E-cadherin polynucleotides in a sample of tumor cells from a subject having lung cancer that is resistant to gefitinib, and selecting the patient as being predicted to benefit from therapeutic administration of gefitinib if the level of E-cadherin polynucleotides in the sample of tumor cells from said patient is higher than the level of E-cadherin polynucleotides in the sample of tumor cells from the subject that is resistant to gefitinib (see page 42, in particular). In regards to claims such as 57, 58, and 74, drawn to methods wherein *any* expression of E-cadherin is predictive of a benefit from EGFR inhibitor, it is noted that the specification discloses that *both* gefitinib-sensitive and gefitinib-resistant patients express E-cadherin polynucleotides (see page 42, in particular). Therefore, the specification provides clear evidence that the claimed methods are not enabled in commensurate with the scope of the claims.

The level of unpredictability for using a particular molecule to identify a patient that would be responsive to a particular therapy is quite high. The state of the prior art dictates that if a molecule such as E-cadherin polynucleotide is to be predictably used as a surrogate for a particular diseased state (such as a non-small cell lung cancer patient who is predicted to benefit from therapeutic administration of gefitinib), one must

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demonstrate a particular expression pattern of E-cadherin polynucleotide correlates with said particular diseased state. For example, Tockman et al (Cancer Res., 1992, 52:2711s-2718s) teach considerations necessary in bringing a cancer biomarker (intermediate end point marker) to successful application. While Tockman et al is drawn to using a particular biomarker to diagnose a particular disease, the teachings of Tockman et al exemplify the state of the prior art for using a particular molecule to indicate a particular diseased state. In the instant situation, the particular diseased state is a cancer that is resistant or responsive to a particular type of therapy. Tockman et al teaches that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in prospective population trials (see abstract). Early stage markers of carcinogenesis have clear biological plausibility as markers of preclinical cancer and if validated (emphasis added) can be used for population screening (p. 2713s, col 1). The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome. Absent evidence of a correlation between a particular expression pattern of a particular molecule and a particular diseased state, one of skill in the art would not predict that said particular expression pattern of said particular molecule is indicative of said particular diseased state without undue experimentation. Such experimentation would in itself be inventive.

One cannot extrapolate the teachings of the specification to the scope of the claims because the claims are broadly drawn to (1) methods to select a lung cancer patient who is predicted to benefit from therapeutic administration of an EGFR inhibitor selected from the group consisting of gefitinib and erlotinib comprising (a) detecting in a sample of tumor cells from just any patient to be tested (including those without lung cancer), the expression of E-cadherin polynucleotides, (b) comparing the level of expression of E-cadherin polynucleotides detected in the patient sample to a level of expression of E-cadherin polynucleotides that has been correlated with just any type of disorder or condition that has been correlated with sensitivity or resistance to the EGFR inhibitor, and (c) selecting the patient as being predicted to benefit from therapeutic administration of the EGFR inhibitor selected from the group consisting of gefitinib and erlotinib if the expression level of the E-cadherin polynucleotides in the patient's tumor cells is statistically more similar to the expression level of the E-cadherin polynucleotides that has been correlated with sensitivity to the EGFR inhibitor than to resistance to the EGFR inhibitor (see claim 66) and (2) methods of selecting a lung cancer patient who is predicted to benefit from therapeutic administration of an EGFR inhibitor selected from the group consisting of gefitinib and erlotinib comprising selecting just any type of patient with tumor cells expressing any amount of E-cadherin polynucleotide as predicted to benefit from therapeutic administration of the EGFR inhibitor (see claim 57), and Applicant has not enabled said methods because it has not been shown that a level of E-cadherin polynucleotides found in tumor cells from just any type of patient which is similar to a level of E-cadherin polynucleotides in just any type

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of sample from just any type of source which has been correlated with sensitivity to gefitinib or erlotinib indicates said patient is sensitive to gefitinib or erlotinib. Further, Applicant has not demonstrated that just any amount of E-cadherin polynucleotide in tumor cells indicates therapeutic benefit to erlotinib or gefitinib.

In view of the teachings above and the lack of guidance, workable examples and or exemplification in the specification, it would require undue experimentation by one of skill in the art to determine with any predictability, that the method would function as broadly claimed.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 48, 49, 53, 55-58, 66, 67, 73, 74, and 76-81 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable

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over claims 1-10 of copending Application No. 11/781946. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-10 of copending Application No. 11/781946 are species of instant claims 48, 49, 53, 55-58, 66, 67, 73, 74, and 76-81.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Summary

No claim is allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SEAN E. AEDER whose telephone number is (571)272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sean E Aeder/
Primary Examiner, Art Unit 1642